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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER

OUSLEY, A

ART UNIT

PAPER NUMBER

1636

DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action SummaryApplication No.
09/458,779

Applicant(s)

Latterich et al.

Examiner

Andrea OusleyGroup Art Unit
1636☐ Responsive to communication(s) filed on _____.☐ This action is **FINAL**.☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims☒ Claim(s) 1-42 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.☒ Claim(s) 1-42 is/are rejected.☐ Claim(s) _____ is/are objected to.☐ Claims _____ are subject to restriction or election requirement.**Application Papers**☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.☐ The drawing(s) filed on _____ is/are objected to by the Examiner.☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.☒ The specification is objected to by the Examiner.☐ The oath or declaration is objected to by the Examiner.**Priority under 35 U.S.C. § 119**☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.☐ received in Application No. (Series Code/Serial Number) _____.☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).**Attachment(s)**☒ Notice of References Cited, PTO-892☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____☐ Interview Summary, PTO-413☒ Notice of Draftsperson's Patent Drawing Review, PTO-948☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

1. This action is in response to the application filed December 10, 1999.
2. Claims 1-42 are pending in the instant application.

Specification

3. The specification is objected to because of the following informalities:

Frequently, applications are filed containing drawings with several views of the invention where the views are labeled using a number-letter combination; for example, the drawings may contain figures labeled "Fig. 1 * >A < ", and "Fig. 1 * >B < ", but the specification describes a "Fig. 1 *". In virtually all of these cases, there is no "Figure 1" missing. Instead, the reference in the specification to the figure is a typographical error, that is, the specification should read "Figures 1A-1*>B < " instead of "Figure 1". Application Division will not treat an application as being incomplete if a figure which is referred to in the specification by a particular number cannot be located among the drawings, if the drawings contain at least one figure labeled with that particular number in combination with a letter. For example, an application will not be treated as incomplete if "Figure 1" is mentioned in the specification (in either the brief or detailed description), but the drawings contain figures labeled "Fig. 1A", "Fig. 1B, etc. The error which exists in the specification should be corrected, however. Application Division will treat an application as incomplete in all other instances where a drawing figure is mentioned in the specification, but the figure is not present in the drawings filed.

In the specification, figures should be referred to in a manner consistent with how the Figures themselves are labeled. Appropriate correction is required for Figures 1A and 1B and Figures 3A and 3B.

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Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-30, 35, and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide comprising a sequence encoding a functional vesicular fusion factor 2 protein (Vff2p), or wherein the protein is as recited in claims 2, 3 or 5, or wherein the nucleotide sequence is as recited in claim 4, or wherein said polynucleotide sequence is linked to a promoter or further comprises a sequence encoding a target protein (or protein of interest) as recited in claims 7-10, or for an expression vector as recited in claims 13-21, or for a host cell as recited in claims 24-30, or an isolated Vff2p protein or the protein of claim 36, wherein Vff2p protein is encoded by the nucleotide sequence of SEQ ID NO. 1 and the amino acid sequence of or any nucleotide sequence encoding SEQ ID NO. 2, and wherein the host cell is *S. cerevisiae*, does not reasonably provide enablement for said polynucleotide, expression vector, host cell, or isolated protein wherein said Vff2p protein is encoded by any nucleotide sequence *other than* SEQ ID NO. 1, any nucleotide sequence *other than* one encoding SEQ ID NO. 2, or any amino acid sequence *other than* SEQ ID NO. 2, and wherein the host cell is any species *other than S. cerevisiae*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

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6. Claims 1-30, 35, and 36 are drawn to a polynucleotide, expression vector, host cell, or isolated protein with further limitations as recited above. The following factors have been considered in formulation of this rejection (*In re Wands*, 858F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988)): the breadth of the claims, the nature of the invention, the state of the prior art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

7. The claims are broad in that they are drawn to any polynucleotide or expression vector comprising any structural or functional homolog of Vff2p, to any target protein or protein of interest, or to any host cell comprising said polynucleotide or homolog, or to any isolated Vff2p protein, which includes structural and functional homologs.

The nature of the invention is as discussed in 5 and 6 above.

An analysis of the prior art indicates that at the time the present invention was made one of skill in that art did not know how to make and/or use a Vff2p polynucleotide, expression vector, host cell, or Vff2p isolated protein, wherein said polynucleotide or protein was other than that identified by SEQ ID NOs 1 and 2, respectively, or by said polynucleotide encoding SEQ ID NO. 2, and wherein the host cell is any species other than *S. cerevisiae*.

The relative skill of those in the art of recombinant engineering and protein expression in yeast is high.

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The area of the invention is unpredictable. As indicated above, one of skill in the art could not predictably carry out the invention in its full scope based on knowledge in the prior art. While some cellular components of the secretory and membrane fusion apparatus are able to function in a heterologous system (*ie.* page 3 of the specification), this is no indication that this will also be the case for Vff2P. In fact on page 11 of the specification applicant admits that the % identity for sequences in other species that may be homologous to Vff2p is rather low. Further, there is no evidence that said putative homologous sequences will have a similar function.

The specification provides insufficient direction or guidance to support the claimed invention in its full scope. The specification does not teach any other Vff2p homologs from any other species or provide convincing evidence that homologs/orthologs exist in other species.

The working examples only relate to Vff2p as identified by SEQ ID NOs 1 and 2, and wherein the host cell is *S. cerevisiae*.

The invention as claimed lacks features that are required to practice the invention in its full scope. As neither the specification nor the prior art provides guidance about how to practice the invention, the quantity of experimentation necessary to carry out the invention in its full scope is high. One of ordinary skill in the art could not rely on the prior art or the specification to teach how to carry out the invention. Therefore, one of skill in the art would turn to "trial and error" to practice the invention, and such experimentation represents undue experimentation.

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8. Claims 31-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.
9. Claims 31-34 are drawn to a method for increasing protein production in or protein secretion from a cell, comprising introducing Vff2p to a host cell, or to said method wherein said cell is cultured under appropriate conditions. The following factors have been considered in formulation of this rejection (*In re Wands*, 858F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988)): the breadth of the claims, the nature of the invention, the state of the prior art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.
10. The claims are broad in that they are drawn to a method of increasing production in or secretion of any protein from any host cell, comprising introducing any structural or functional homolog of said Vff2p into said cell.

The nature of the invention is as discussed in 9 above.

An analysis of the prior art indicates that at the time the present invention was made one of skill in that art did not know how to make and/or use a Vff2p polynucleotide, host cell, or isolated Vff2p protein, wherein said polynucleotide or protein was other than that identified by SEQ ID NOs 1 and 2, and wherein the host cell is any species other than *S. cerevisiae*. Further, even though the specification discloses making and using said Vff2p polynucleotide and a host

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cell containing said polynucleotide, there is no evidence that said method using Vff2p actually increases protein production in or protein secretion from the host cell used. The data in Figures 3A and 3B indicates only that the growth rate is increased in a host cell containing Vff2p. Thus, the *overall* protein production/unit of time is increased, but an increase in the level of protein production *within* a cell or protein secretion *from* a cell is not disclosed.

The relative skill of those in the art of expression of proteins in yeast is high.

The area of the invention is unpredictable. As indicated above, one of skill in the art could not predictably carry out the invention in its full scope based on knowledge in the prior art. See 7 above for discussion of structural or functional homologs of Vff2p not disclosed in the instant application. More importantly, there is no evidence that using even the Vff2p disclosed will increase protein production in or secretion from a host cell. See Romanos et al., Yeast 8: 423-488, 1992 for discussion of unpredictability in production of intracellular proteins in and secretion of proteins from yeast, and expression of proteins in non-*Saccharomyces* yeasts.

The specification provides insufficient direction or guidance to support the claimed invention in its full scope. The specification does not teach any other Vff2p homologs from any other species, and does not teach a method of increased protein production or secretion.

The working examples only relate to Vff2p as identified by SEQ ID NOs 1 and 2, and wherein the host cell is *S. cerevisiae*, and do not demonstrate increased protein production or secretion.

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The invention as claimed lacks features that are required to practice the invention. As neither the specification nor the prior art provides guidance about how to practice the invention, the quantity of experimentation necessary to carry out the invention is its full scope is high. One of ordinary skill in the art could not rely on the prior art or the specification to teach how to carry out the invention. Therefore, one of skill in the art would turn to "trial and error" to practice the invention, and such experimentation represents undue experimentation.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 6-11, 12, 17-22, 32, 34, and 36-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claims 6, 7, 11, 17, 18, and 22 are indefinite for recitation of "first promoter" as there is no mention of another promoter in said claims.

14. Claims 8-10, 19-21, and 42 are indefinite for recitation of "a [or] the target protein" as it is unclear if said term refers to the "Protein X" of Figures 1A and 1B, *ie.* to any protein of interest, or possibly in claims 9, 20, and 21 to Vff2p. Further, the term "target protein" implies a set of proteins that is more narrow in scope than the set of proteins including *any* protein of interest. Claims 9, 10, 20, and 21 recite the limitation "the target protein". There is insufficient antecedent basis for this limitation in the claims.

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15. Claim 12 recites "yeast". There is insufficient antecedent basis for this limitation in the claims.

16. Claim 36 is indefinite for recitation of "essentially corresponding" as it is unclear what level of structural and/or functional similarity this would encompass, and by what method determined.

17. Claims 31 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: culturing said cell.

18. Claims 37-42 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a step for constructing the recombinant cell, a step for inducing mutagenesis, prior to the recited step of selecting for temperature-sensitive mutants by growing at a high temperature.

19. Claims 32 and 34 recite the limitation "the host cell". There is insufficient antecedent basis for this limitation in the claims.

20. Claims 37-42 recite the limitation "the recombinant cell". There is insufficient antecedent basis for this limitation in the claims.

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Conclusion


21. Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. For FAX transmissions in cases in which the examiner has been notified by phone to expect the transmission, the FAX number is (703) 305-7939. In such cases please call the examiner at (703) 305-6915 at the time of transmission to expedite delivery of the fax. The faxing of such papers must conform with the notices published in Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrea Ousley, Ph.D. whose telephone number is (703) 305-6915. The examiner can normally be reached on Monday through Friday from 9 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, Ph.D., can be reached at (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the group receptionist whose telephone number is (703) 308-0196.

Andrea Ousley, Ph.D.

Patent Examiner


ROBERT A. SCHWARTZMAN
PATENT EXAMINER